Deprescribing medicines in older people living with multimorbidity and polypharmacy: the TAILOR evidence synthesis

Joanne Reeve,[1*] Michelle Maden,[2] Ruaraidh Hill,[2] Amadea Turk,[3] Kamal Mahtani,[3] Geoff Wong,[3] Dan Lasserson,[4] Janet Krska,[5] Dee Mangin,[6] Richard Byng,[7] Emma Wallace[8] and Ed Ranson[9]

[1]Academy of Primary Care, Hull York Medical School, University of Hull, Hull, UK
[2]Liverpool Reviews and Implementation Group, Institute of Population Health, University of Liverpool, Liverpool, UK
[3]Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK
[4]Health Sciences, Warwick Medical School, University of Warwick, Coventry, UK
[5]Medway School of Pharmacy, Universities of Greenwich and Kent, Chatham, UK
[6]Department of Family Medicine, McMaster University, Hamilton, ON, Canada
[7]Community and Primary Care Research Group, Peninsula Medical School, University of Plymouth, Plymouth, UK
[8]Department of General Practice, RCSI University of Medicine and Health Sciences, Dublin, Ireland
[9]Liverpool, UK

*Corresponding author Joanne.Reeve@hyms.ac.uk

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Scientific summary

The TAILOR evidence synthesis

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Scientific summary

Background

Polypharmacy is common practice in modern health care, offering benefits to many patients. However, a 2013 report by The King's Fund [Duerden M, Avery A, Payne R. *Polypharmacy and Medicines Optimisation*. 2003. URL: www.kingsfund.org.uk/sites/files/kf/field/field_publication_file/polypharmacy-and-medicines-optimisation-kingsfund-nov13.pdf (accessed 16 June 2021)] identified a growing challenge from problematic polypharmacy: when (potential) harms from medicines outweigh (potential) benefits. The report recommended that deprescribing (the planned/supervised reduction in dose or stopping of medicines that might be causing harm or no longer providing benefit) be recognised as an important component in optimising the use of medicines in a polypharmacy context. The report's authors called for practice to be tailored to individual circumstances. The need for new evidence to support patient-centred understanding of deprescribing practice was identified.

Previous research has demonstrated that although clinicians and patients potentially support deprescribing, both feel unconfident in knowing how and when to make these changes. Guidance on stopping longer-term, potentially inappropriate, medicines has been around for a number of years [e.g. Beers criteria, the Screening Tool of Older Person's Prescriptions/Screening Tool to Alert doctors to the Right Treatment (STOPP/START) tool]. However, a particular challenge comes in knowing how and when to stop medication that may be seen as 'appropriate' from a clinical perspective (including condition-specific guidelines) but potentially 'not right for this individual' as judged by the patient or their clinician.

An additional challenge comes in managing the process of withdrawal, including understanding issues of safety. There is no comprehensive data set describing the effects on safety and the clinical impact of stopping medication. A third barrier comes from organisational factors, such as the design of health-care systems and performance management processes, that inhibit clinicians from tackling problematic polypharmacy through providing tailored care. Specifically, clinicians lack the evidence-based support that addresses 'permission' (why you could tailor care) and professional skills and confidence (how you could tailor care).

To tackle problematic polypharmacy, therefore, we need data on the safety and impact of deprescribing, and a framework describing good practice. This translates into two research questions:

1. What quantitative and qualitative evidence exists to support the safe, effective and acceptable stopping of medication in older people with multimorbidity and polypharmacy?
2. How, for whom and in what contexts can the safe and effective individual tailoring of clinical decisions related to medication use work to produce desired outcomes?

Design

Our funders requested a secondary analysis of published data for this work. We therefore described the need for two distinct review methods to answer our questions and so generated three objectives for the TAILOR project:

1. to complete a robust scoping review of the literature on stopping medicines in this group to describe what is being done, where and to what effect
2. to undertake a realist synthesis review to construct a programme theory explaining the mechanisms and heterogeneity of deprescribing approaches
3. to use the findings to inform practice, research and policy.

Methods

Scoping review

Data sources

We conducted comprehensive searches in MEDLINE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Web of Science, EMBASE, Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials), Joanna Briggs Institute Database of Systematic Reviews and Implementation Reports, Google (Google Inc., Mountain View, CA, USA) and Google Scholar (targeted searches for both Google sources).

Search

We used a comprehensive, broad and iterative approach to identify relevant literature. We conducted an initial exploratory search using search terms identified by the review team and PubMed PubReMiner in MEDLINE (via Ovid).

Our inclusion criteria were:

- population – patients (aged ≥ 50 years), with polypharmacy (five or more medicines per day) and multimorbidity (two or more long-term conditions); and health-care professionals involved in deprescribing for this group
- interventions – strategy or strategies used to safely deprescribe medications in older people with multimorbidity and polypharmacy; outcomes related to effectiveness, safety and acceptability
- context – any
- study design – quantitative, observational or qualitative methodologies
- limits – from 2009 (our preliminary search identified no abstracts on deprescribing before this date), English language and no conference abstracts.

We refined a draft search strategy through a sensitivity analysis and peer review. We conducted a comprehensive search on 30 August 2019 and then updated this on 23 June 2020 with the addition to the search of 'five or more' as a free-text term in the polypharmacy concept. An experienced information specialist (MM) conducted the searches.

Data extraction and assessment of validity

Data were extracted on study design, population characteristics, health inequalities (using the PROGnosis RESearch Strategy partnership+ framework), intervention characteristics and outcomes of interest. The template was piloted and all data were extracted by two reviewers (MM and Katherine Edwards) independently and cross-checked using Microsoft Access® (Microsoft Corporation, Redmond, WA, USA).

No formal measure of study quality was applied, as per recognised practice in scoping reviews.

Synthesis

The synthesis followed the scoping review methodology set out by the Joanna Briggs Institute (Peters MDJ, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. *Int J Evid Based Healthc* 2015;**13**:141–6). Five steps are described: (1) setting the research question, (2) identifying studies, (3) selecting studies, (4) charting the data and (5) collating and reporting.

Realist review

Data sources

Data sources comprised Ovid MEDLINE, EMBASE, CINAHL, The Cochrane Library (including the Cochrane Central Register of Controlled Trials and Database of Abstracts of Reviews of Effects),

Cochrane Effective Practice and Organisation of Care Group Specialised Register, Campbell Collaboration Library of Systematic Reviews, Joanna Briggs Institute Database of Systematic Reviews and Implementation Reports, PsycInfo, Allied and Complementary Medicine Database and CAB Abstracts, trial registries, grey literature including Google, and websites of relevant stakeholders.

Search

A comprehensive, structured approach was adopted, recognising Petticrew's guidance [Petticrew M. *Complex Interventions: Some Definitions, Examples and* Challenges. URL: www.evidencebasedpublichealth.de/download/Complex_interventions_Petticrew.pdf (accessed 16 June 2021)] that complex intervention search strategies need to adopt broader eligibility criteria than those used in traditional systematic reviews, going beyond participants, interventions, comparisons, outcomes, study design to include context, processes and theory (i.e. mechanisms of action). This was in addition to Peters *et al.*'s call (Peters MDJ, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. *Int J Evid Based Healthc* 201;**S13**:141–6) for scoping reviews to consider populations (i.e. types of participants), context, and 'concepts' (i.e. the interventions being examined and the outcomes used to assess their success).

The inclusion/exclusion criteria were:

- population – people aged ≥ 50 years with two or more long-term conditions and five or more medicines per day, excluding participants from studies focused on managing acute toxicity
- interventions – any systematic intervention process used to safely withdraw medicines, excluding those without a comparator group
- context – any suitable setting
- study design – any comparative study, excluding single case reports or case series.

Data extraction and assessment of validity

First screening applied inclusion/exclusion criteria at title and abstract level (by AT, with 10% independently reviewed by KM/GW). Subsequent selection of full-text documents primarily focused on the extent to which the articles included data that could contribute to the development and refinement of the programme theory. Documents that did not include a mention of involvement from patients in the deprescribing/medication management process were deemed to be of little relevance given our focus on individually tailored approaches to medication management.

Synthesis

The synthesis followed the methodological and publication standards for realist reviews described by the Realist And Meta-narrative Evidence Syntheses: Evolving Standards (RAMESES) group. This review followed the key steps of conducting a realist review outlined by Pawson *et al.*: [Pawson R, Greenhalgh T, Harvey G, Walshe K. Realist review – a new method of systematic review designed for complex policy interventions. *J Health Serv Res Policy* 2005;**10**(**Suppl. 1**):21–34] clarifying the scope, searching for the evidence, selecting articles, extracting and organising data, synthesising the evidence and drawing conclusions.

Following initial broad descriptive coding of the data to make sense of the landscape, we developed context–mechanism–outcome configurations (CMOCs). This process began by considering an outcome and then using interpretations of the data to develop explanations of how specific contexts might have triggered different mechanisms to produce that outcome. A list of potential CMOCs was created by Amadea Turk and then shared and discussed with Geoff Wong, Joanna Reeve and Kamal Mahtani as well as with our patient and public involvement partners (ER). Developing CMOCs were then incorporated into the refined programme theory. This process continued iteratively to develop CMOCs that explained what we judged were the most important parts of the programme theory. CMOCs were considered to have sufficient explanatory value when they were able to account for as many as possible of the data related to that CMOC, had as few ad hoc exceptions as possible, and fitted in with existing theories that explained similar phenomena, namely the conditions of consilience, simplicity and analogy, respectively.

Results

Scoping review

Setting the research question
We sought to identify (1) what research methods (study designs) have been used in the studies that focus on this topic; (2) what clinical strategies, contexts and outcomes have been studied; and (3) what tools are available to support addressing problematic pharmacy in older people with multimorbidity and polypharmacy.

Identifying and selecting studies
A total of 17,160 abstracts were initially identified by the search: 9529 once duplicates were removed. A total of 8847 were removed at the screening of titles and abstracts, and a further 662 were removed at the full-text review. Our scoping review found that, between 2009 and 2020, 20 studies (reported in 27 references) examined the effectiveness, safety and acceptability of deprescribing in older adults (aged $\geq$ 50 years) with polypharmacy (five or more prescribed medications) and multimorbidity (two or more conditions).

Charting the data
We used a modified Template for Intervention Description and Replication (TIDieR) framework to describe the data.

Collating and reporting
Our findings revealed considerable heterogeneity in the study designs used, the study population and duration, and the definitions of multimorbidity applied. Most studies were small to moderate in size with a short follow-up (all $<$ 1 year, and 30% having a follow-up of $\leq$ 3 months). Owing to the complex nature of the deprescribing interventions employed, the TIDieR framework was found to be insufficient on its own in allowing for a rich description of the deprescribing strategies. Specifically, this related to the lack of a detailed description of the deprescribing intervention components. Therefore, we used a novel approach in supplementing the TIDieR framework with Reeve *et al.*'s deprescribing process framework. This described seven steps needed to support robust deprescribing practice: (1) a comprehensive medical history, (2) assessment of risk/harm, (3) identification of potentially inappropriate medicines, (4) shared decision on whether or not to stop, (5) communicate a plan, (6) implement and monitor, and (7) document the process.

Using this approach, our findings demonstrated that studies used multiple outcomes relating to the effectiveness, safety and acceptability of interventions. Altogether, 454 outcomes were reported: effectiveness ($n = 382$), acceptability ($n = 49$) and safety ($n = 23$). We described considerable variation in the reported effects of deprescribing with both improvement and decline in reported outcomes. Interventions were generally acceptable to clinicians, although patient perspectives were commonly not reported. Reporting of safety outcomes was generally positive, although concerns were flagged for general clinical outcomes in secondary care-based studies in which no clinical tools were used. Safety outcomes were reported only for clinician-led interventions and not for pharmacist-led interventions. We conclude that our map of the evidence offers clinicians evidence-informed support for the safety, clinician acceptability and potential effectiveness of deprescribing approaches that demonstrate structured approaches to deprescribing decisions.

Realist review
A total of 2602 abstracts were identified from our database search: 2297 were excluded at screening on inclusion/exclusion criteria, and 202 were excluded at the full-text review because of low relevance. A total of 119 abstracts were included in the final review.

Our initial analysis identified two broad themes: the deprescribing landscape (context), and enhancing deprescribing (mechanisms). Both recognised the significant intellectual and emotional effort involved in the knowledge work of making beyond-protocol decisions about medicines, work that acts as a barrier to tailored prescribing.

Application of the realist method generated 34 CMOC statements, grouped under eight headings.

Tailored deprescribing is affected by the following:

- organisational and system factors – five CMOCs related to clinical guidelines, transitions in care and access to information, and unclear roles and responsibilities
- health-care professional factors – six CMOCs related to skills and experience, professional etiquette and time
- patient factors – eight CMOCs related to perceived value of medicines and the influence of family and carers.

Four potential interventional strategies to improve deprescribing practice were recognised:

1. shared decision-making (three CMOCs)
2. continuity of care and development of trust (five CMOCs)
3. monitoring (four CMOCs)
4. multidisciplinary teams (three CMOCs).

Our final programme theory described/explained the components needed to reduce the cognitive/emotional load to enable tailored (de)prescribing practice. These components were the presence of an enabling infrastructure (including clarity of professional roles, building professional skills and confidence, recognising the value of distinct generalist and specialist skills within a multidisciplinary team, supporting continuity of approach and addressing incentive structures); consistent access to the high-quality (including contextual) data needed for tailored decisions; support for the generation of shared understanding of the meaning/purpose of medicines, enabling tailored explanations of medicines use; and the ongoing monitoring of effect (continuity of support), contributing to establishing and maintaining trust. Our findings extend existing models of good practice by recognising the need to consider the impact of prescribing decisions beyond biomedical/pharmacological effects, and by demonstrating the need to include organisational/contextual factors in models of best practice.

Discussion

Our analysis revealed that deprescribing under 'research conditions' mapped well to expert guidance on the steps needed for good clinical practice. When reported, interventions were generally safe and commonly reported as acceptable to clinicians, although fewer data were available on acceptability to patients. Reported patient outcomes were highly variable in terms of both what was measured and the observed size of effect.

Our scoping review confirms that deprescribing is a complex (non-linear) intervention: an interpretive practice that occurs in the interaction between patient and practitioner to generate a tailored understanding of priorities (including the meaning and value of medicines) and possibilities. It is the generation of a tailored explanation of medicines use in context that is necessary for effective care, required also to support and maintain the trust that is needed to sustain management of complex health-care needs and so optimise outcomes.

Our work demonstrates the importance and value of theory-informed research to support complex clinical practice. By combining the theory-based outcomes of the realist review with an assessment of

the empirical/quantitative outcomes of the scoping review, we are better able to make recommendations for future practice.

Our analysis highlighted two key challenges for the research community to consider in generating evidence to support patient outcomes and clinical practice. First, we recognised the need for research that recognises, and examines, deprescribing in context. Second, our review highlighted the challenges in synthesising data (whether as a clinician or a researcher) from such a fragmented research base. In the absence of a clear reference point defining what research is needed and what outcomes matter, we generated a data set that is hard to interpret meaningfully.

Conclusions and implications for research and practice

We can therefore conclude that the map of the data offers clinicians evidence-informed support for the safety, clinician acceptability and potential effectiveness of deprescribing approaches that demonstrate structured approaches to deprescribing decisions. Our review recognises the importance of generating practice-based evidence for complex health care, and raises questions for the research community about how we best achieve that. Our TAILOR deprescribing framework extends existing models of good practice by demonstrating the need to include organisational/contextual factors in models of better practice.

We recognise three implications for practice:

1. Deprescribing processes using explicit approaches to decision-making are often safe and acceptable to clinicians. However, clinical judgement will always be necessary.
2. Deprescribing is a complex form of clinical work and practices may want to review their medication review practice in the light of our findings.
3. TAILOR provides clinicians with an evidence-based understanding of how and why the generation and maintenance of trust, including through maintaining continuing care, is essential for deprescribing practice.

We describe three recommendations for research:

1. Future research into deprescribing recognises the need for theory-grounded, complex intervention research methodologies in order to generate knowledge for practice.
2. The research community considers how to improve the co-ordination and consistency of research in this area to optimise the potential for/impact of synthesis work.
3. Researchers optimise the impact of working with patient and public involvement partners through prioritising work to develop and maintain their contextual understanding of how research activity can have an impact on care.

Study registration

This study is registered as PROSPERO CRD42018107544 and PROSPERO CRD42018104176.

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This report

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